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THE SOURCE AND TRANSMISSION OF NASOPHARYNGEAL INFECTIONS DUE TO CERTAIN BACTERIA AND VIRUSES

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In view of the interest now being taken in the possibilities of ultra-violet light and aerosols for the prevention of nasopharyngeal infections, this paper discusses the probable methods by which the bacterial and virus infections of the nasopharynx are disseminated. For various reasons only scarlet fever, tonsillitis, pneumonia, diphtheria, and meningitis will be considered among those due to bacteria ; and of those caused by viruses, only influenza, measles, and the common cold (it being freely admitted that direct proof of the virus origin of the last is still wanting).

Spread of Bacterial Infections

There is abundant evidence that preceding an outbreak of bacterial infection of the nasopharynx a slow increase occurs in the carrier rate, and not until this has reached a certain level do clinical cases appear. In the course of this, it may be assumed that, in general, the infecting bacteria reach the recipient in the air he breathes and gain access to the atmosphere from the nose or mouth of the case or carrier. The presence of the specific organisms in the air may arise in two ways: (1) by expulsion of the organisms from the nose or mouth when the case or carrier indulges in such activities as speaking, coughing, sneezing, blowing, or spitting ; and (2) by contamination of the hands, handkerchief, pillow, bedding, towels, or any other object which has access to the secretions of the mouth or nose and from which they can be released after the secretions have dried. These two mechanisms must be discussed separately.

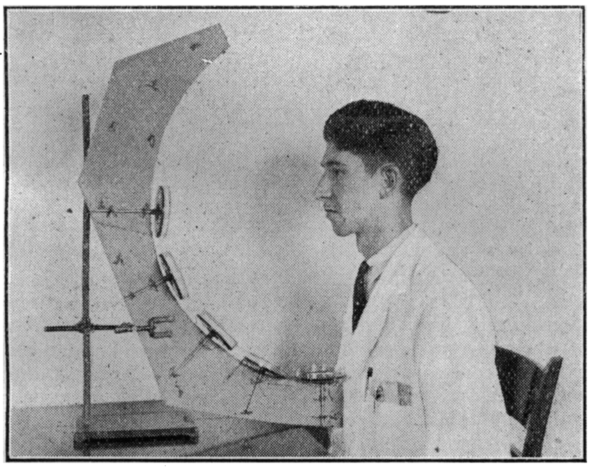

FIG. 1

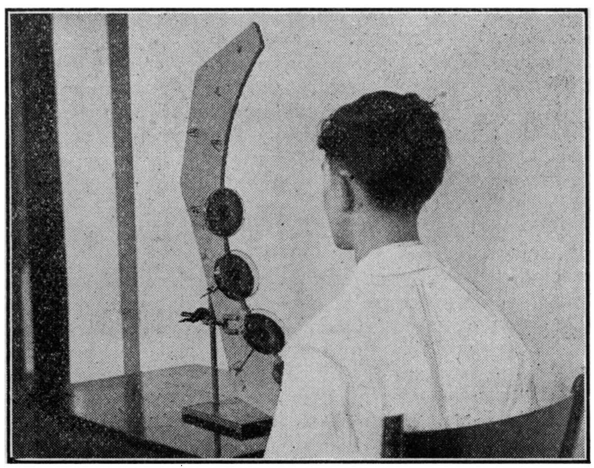

FIG. 2

Expulsion from Nose or Mouth

In experiments, which need not be quoted in detail, it has been determined that few organisms reach the atmosphere when the subject breathes quietly, but that the number rapidly increases when he carries on some form of nasopharyngeal activity. Even so, the great majority of the expelled organisms come from the mouth, few or none coming from the nose. The mechanism of expulsion itself has been recently reviewed in detail by Duguid (1945), while Hare (1940) described experiments which indicated the path followed by the organisms after leaving the mouth. These experiments have been repeated and extended. In brief, the method employed is as follows.

A subject sits upright in a quiet room and counts for five minutes, coughs six times, sneezes once, or blows for two minutes directly forwards with his mouth in the centre of a quarter circle of culture plates. In most experiments the circle has been twelve inches (30 cm.) in radius (Figs. 1 and 2). The plates are situated on the radii at 90°, 67.5°, 45°, 22.5°, and 0° from the vertical, the first-named being directly in front of the mouth and the last directly under it, all of them twelve inches away. After incubation, the number of colonies on the plates are counted. The collected results are given in Table I.

TABLE I.—*Average Number of Colonies per Person on Culture Plates Exposed at Different Positions in Relation to the Mouth*

Position of Culture Plate	Talking		Coughing		Blowing		Sneezing	
	Average	% of Total	Average	% of Total	Average	% of Total	Average	% of Total
0° ..	28·1	30·0	6·7	4·9	1·3	2·6	355·8	7·5
22·5° ..	39·1	41·8	8·9	6·5	1·6	3·2	1,636·0	34·4
45° ..	16·2	17·3	60·1	43·9	8·0	16·0	2,425·6	51·1
67·5° ..	8·4	9·0	52·9	38·7	27·0	54·2	262·8	5·5
90° ..	1·8	1·9	8·2	6·0	12·0	24·0	71·3	1·5
Total ..	93·6	100·0	136·8	100·0	49·9	100·0	4,751·5	100·0
Number of subjects	39		20		3		9	

It is not suggested that all the expelled organisms appear as colonies on the plates, but the method does give an indication of the route they take after leaving the mouth. For this reason it would appear that the great majority of the organisms are in droplets of fairly large size whose trajectory depends on the resultant of the force of gravity acting perpendicularly to their initial motion and on the amount of force used in expelling them. Naturally the trajectory is somewhat flatter when violent methods of expulsion are used than when talking, the result being that the majority of the organisms were on the plate at 67.5° from the vertical when blowing, on those at 67.5° and 45° when coughing, on those at 45° and 22.5° when sneezing, and on the plates at 22.5° and 0° (directly under the mouth) when talking.

In the above experiments the head was in the natural position, but if it be inclined forwards so that the mouth is pointing directly downwards over the plate at 0°, gravity assists the force of expulsion and quite large numbers of organisms can be isolated on that plate. If, on the other hand, the mouth faces upwards, very few organisms travel any distance at all, most of them apparently falling back on to the face.

Thus it is obvious that gravity exerts a very powerful influence on the droplets, the great majority of those which contain organisms falling downwards shortly after they leave the mouth. The ultimate fate of the organisms therefore depends on the position and the surroundings of the donor as well as the force exerted in expelling them. While sitting at a desk or table, lying in bed or in similar positions, a very high proportion of the total output will impinge on some surface below the mouth, and only by the more violent methods will it be possible to avoid this and obtain droplets with a flat enough trajectory to float free before becoming "neutralized" by falling on some such surface. Some idea of the numbers which may be expected to do this may be gained from the number of colonies obtained on the plate at 90°, directly in front of the mouth. As will be seen from Table I, the largest number was obtained with the subject sneezing—71.3 colonies (though, had not the subjects unanimously jerked their heads downwards, it might have been larger)—and was smallest when talking, only 1.8 colonies being obtained. When these figures are compared with the 4,061.6 colonies obtained on the plates at 22.5° and 45° when sneezing, and the 67.2 obtained on the plates at 0° and 22.5° when talking, it is obvious that under most circumstances the vast majority of the droplets containing organisms will be "neutralized" by falling on to some object below the mouth.

When the subject is standing upright, however, with from four to six feet (120–180 cm.) of air below the level of his mouth, some of the droplets will be neutralized by falling on to his clothes, some by falling direct to the ground; but many will rapidly lose water by evaporation, leaving their salts, non-volatile substances, and bacteria as droplet nuclei (Wells, 1934). These are so small that the force of gravity is unable to overcome the resistance of the air, and in consequence they float free. The number of droplet nuclei produced, as well as the number which contain organisms, will naturally depend on the particular activity of the subject. Some idea of the extent of bacterial pollution of the atmosphere which can occur in this way may be obtained from the following type of experiment.

The nose and mouth of a subject were projected into a large box, 51 in. (130 cm.) high, 32 in. (80 cm.) wide, and 21½ in. (55 cm.) deep, the mouth being placed 24 in. (60 cm.) from the floor. The walls and floor were covered with muslin soaked in liquid paraffin to neutralize the larger droplets falling on them. Five blood-agar plates were placed on the floor and exposed for one hour before the activities enumerated below. They were then removed, the subjects talked, coughed, or sneezed, and after an interval of five minutes a second series was inserted through a hole in the wall. They were left for one hour in order to collect the lighter particles slowly settling out from the air. Following incubation at 37° C., the difference between the number of colonies on the two series of plates was assumed to represent the number of nasopharyngeal organisms collected as a result of the particular activity of the donor.

It was found that after talking for five minutes nine normal persons produced an average of 13 colonies, after six coughs 28, and after one sneeze 715. Thus it is obvious that sneezing is by far the most prolific activity, air pollution being quite mild after only talking and coughing. Duguid (1945) used much the same technique but sampled the air directly with a slit sampler, and similarly found that only by sneezing was it possible to obtain any large numbers of the lighter droplets and droplet nuclei containing organisms.

Thus the number of organisms expelled varies according to the violence of the methods used for expelling them; the path they take after leaving the mouth will likewise vary with the particular activity of the donor, but will in general be downwards rather than forwards, and their ultimate fate will depend to a large extent on the position of the mouth in relation to surrounding objects, but will generally involve the deposition of the organisms on some surface below mouth level. Those which do not reach such a surface will float free as infected droplet nuclei. Lastly, it should be pointed out that without sneezing or violent blowing it must be almost impossible for the subject to project any considerable number of organisms into the mouth of another person on the same level and only 12 in. (30 cm.) away.

Expulsion of Specific Organisms by Carriers and Cases

Using the same methods, Hare (1940) studied 12 known carriers of group A haemolytic streptococci. As might be expected, under the influence of gravity these organisms tend to fall away along with the nasopharyngeal saprophytes. But of equal importance is the fact that very few of the colonies on the plates contained the specific organisms. This information is summarized in Table II, in which are given the total number of colonies collected, as well as the number containing haemolytic streptococci isolated at all the sittings in which the heads of the carriers were upright. Seven of the carriers did not expel any haemolytic streptococci during the tests, though three of them expelled some when the head was turned downward. Acutely infected cases were not studied, though several were examined as soon as they were convalescent. But Bloomfield and Felty (1924) encountered considerable difficulty in obtaining expulsion of infected droplets from patients with scarlet fever and tonsillitis during the acute phase of the illness. In a recent paper Duguid (1946) described an investigation of 50 cases of scarlet fever and 37 carriers who coughed six times at blood-agar plates held only 3 in. (7.6 cm.) away from the mouth. About 10% of the total colonies contained haemolytic streptococci, but only 39 out of 87 individuals expelled them.

TABLE II.—*Total Colonies and Those Containing Group A Haemolytic Streptococci Isolated on Plates Exposed at all Sittings with Head Upright*

Carrier	Talking Time (mins.)	Total Cols.	Haemolytic Strep.		No. of Coughs	Total Cols.	Haemolytic Strep.	
—			No.	%			No.	%
Ric	15	386	0	0	18	52	0	0
Tow	10	263	1	0·38	12	32	0	0
Ste	5	153	0	0	6	45	0	0
Sim	5	245	0	0	6	48	0	0
Mac	5	114	0	0	6	84	0	0
Pie	5	54	2	3·6				
Cus	5	114	3	2·63				
Kee	25	198	1	0·51	24	127	0	0
Rol	15	196	1	0·51	18	1,939	2	0·1
Ros	10	48	0	0	6	45	0	0
Mo	10	272	0	0	12	67	0	0
Wat	10	135	0	0	12	71	0	0
Total		2,178	8			2,510	2	

The expulsion of pneumococci and of meningococci does not seem to have been investigated by a similar technique. Teague (1913), however, held serum-agar plates 3 in. from the mouth of patients with diphtheria who were talking and coughing. Only 48 out of 180 plates contained the specific organisms, only 65% of the patients emitted them during the period of test, and in 30 out of 48 patients only one colony per plate was isolated. Similar results were obtained by Duguid (1946) with patients coughing six times at tellurite plates. The specific organisms comprised only 4% of the total output, and they were isolated from only 10 out of 50 patients. No comparable experiments have been carried out with carriers, but, in view of the statement of Copeman *et al.* (1922) that they have very few diphtheria bacilli in their throats, it would seem that the ability of both case and carrier to emit the specific organisms is no better than that of carriers of haemolytic streptococci.

Thus the available evidence suggests that only a proportion of carriers of streptococci and diphtheria bacilli (and patients in the acute stages of infection) expel these organisms, and that the organisms which they do expel will, in most circumstances, fall and impinge on some surface below the level of the mouth. Those which do not will float free as infected droplet nuclei; but in view of the fact that very few droplet nuclei produced as a result of other activities than sneezing contain organisms at all, and the number of specific organisms expelled by a carrier is only a small fraction of the total output, it follows that the production of infected droplet nuclei by carriers of these organisms can hardly be a serious factor in the dissemination of infection.

Much less is known about the expulsion of meningococci and pneumococci, but it may be assumed for the present that it proceeds along the same lines.

Contamination of Person and Surroundings

Working with carriers of haemolytic streptococci, Hare (1941) showed that the skin of the face and hands, the clothing, and the handkerchief may be contaminated by their organisms and that this contamination may persist over long periods of time. The same author, and also Hamburger, Puck, Hamburger, and Johnson (1944), showed that the bedding and the dust of the carriers' rooms are contaminated. There is also evidence that the nasal carrier is more capable of polluting his surroundings than the throat carrier, and Hamburger, Green, and Hamburger (1945) found that the bedding of such carriers might contain 80 times more streptococci than that of throat carriers. Exactly how the organisms reach the person and the bedding has not been determined. It is probable that some reach it during conversation and coughing but that the majority come from nasal or oral secretions directly. However they arrive, there is no doubt that there may be quite marked contamination.

There is also evidence that the organisms may be released into the atmosphere from these situations. Before this can occur the particular secretion must be dry. Using a wind-tunnel, Willits and Hare (1941) showed that lint infected with haemolytic streptococci did not infect the air stream so long as it was moist, or even when dry so long as it was undisturbed. But, once dry, very slight degrees of agitation sufficed to release considerable numbers of organisms into the air stream. For the same reason, it is possible to show that there may be little or no air contamination in the neighbourhood of the bed of a carrier when all is quiet, but that the number of specific organisms in the air increases very considerably if the bed is made or agitated only slightly (Willits and Hare, 1941; Thomas and van den Ende, 1941; Hamburger, Puck, Hamburger, and Johnson, 1944).

Much less evidence is available in respect of the other bacteria, although Stillman (1917) found Types I and II pneumococci in the dust of 48 out of the 183 households in which cases had occurred, but only one Type I in 62 control households. Eagleton (1919) found meningococci in the air of Army huts in which carriers were sleeping. The ability of carriers of diphtheria bacilli to contaminate their surroundings does not appear to have been investigated, although Wright, Shone, and Tucker (1941) found them in the dust of wards in which there were cases.

Mechanism of Transfer from Person to Person

The investigations reported in the preceding section show that, unless extremely violent and impolite methods are employed, it is probably very difficult for a carrier to infect the atmosphere in his vicinity to any great extent directly from his mouth or nose. Furthermore, he is equally unable to infect directly, by any other method short of violent sneezing or blowing, another person whose mouth is only 12 in. (30 cm.) away and on the same level. On the other hand, his person, the objects which surround him, and particularly his bedding, may be contaminated by his organisms, some having presumably reached them from the droplets which have fallen in the course of conversation, etc., but probably a far larger proportion by direct contact with his nasal and buccal secretions. As the organisms on the surrounding objects can reach free air after drying, Hare (1940) suggested that it was these organisms which are responsible for conveying infection to others.

This hypothesis was put forward to explain the transmission of haemolytic streptococcal infections, but there would seem to be little doubt that it also applies in other bacterial infections of the nasopharynx. In view of this, it is to be expected that little or no transfer of infection would occur during ordinary contacts of the day, but that an ill-ventilated office or crowded class-room, and particularly the dormitory, would be the place where infections of this type are acquired. Epidemiological observations confirm this; for the work of Glover (1918) on the spread of meningitis, of Glover and Griffith (1931) and of Dudley (1926) on the spread of streptococcal infections, of Dudley (1926) on the spread of diphtheria, and of Schroder and Cooper (1930) and Strom (1932) on the spread of pneumonia, all point strongly to the importance of the sleeping-place and, to a somewhat less extent, of the class-room in the epidemiology of these infections.

This would seem to be due to the fact that during the day-time the number of infectious particles expelled direct into the atmosphere or released from objects available for contamination seldom reaches dangerous proportions, although something approaching it may occur in class-rooms or offices with closed windows when the clothing is shaken or handkerchiefs are waved about in the air. But in the dormitory a high proportion of the organisms collected on the bedding during the night are released at once when the room awakens and the occupants get up; and, in common with others, we have found that the bacterial population of the air of Army huts increases ten to twenty times following reveille. It is the sudden release of the concentrated output of the night which makes available enough infected particles to increase the number of carriers or bring about clinical infections.

Spread of Virus Infections

It is generally assumed that epidemics of influenza, measles, and the common cold are due to linear spread over the lines of communication, and that a gradual increase in the carrier rate, an apparent prerequisite for the development of an outbreak of bacterial infection, does not occur. However, it has recently been demonstrated that mouse pneumonia virus may remain latent in the tissues of a number of different species of laboratory animals, passing from animal to animal without apparent clinical infection. The virus may be mobilized, however, and cause infection, with the production of specific antibodies, by the application of a suitable non-specific stimulus such as the intranasal instillation of sterile suspensions of egg embryo and similar materials (Eaton and Van Herick, 1944; Horsfall and Curnen, 1946). A slightly different but essentially similar mechanism has been invoked by Shope (1944) to account for the spread of swine influenza. It is possible that something similar occurs in influenza, measles, and the common cold, the latent virus corresponding in some degree to the bacteria in the throat of a carrier.

What the essential change may be which causes the virus to awaken and produce clinically apparent infection is open to conjecture, but in view of the fact that colds, particularly in North America, almost invariably appear immediately after the sudden drop in temperature which heralds the autumn, that, although influenza may occur in the summer, recent epidemics of influenza A and B have been winter diseases in both hemispheres, and that measles usually makes its appearance in the autumn, it would seem that weather may play some part in this.

Nevertheless this does not provide a complete explanation; for if latent virus is widely disseminated before an outbreak it is probably in isolated pockets or cells of the population rather than in a high proportion of the population as a whole. What proportion of the world is seeded in this way, and how far apart the pockets are, are matters for conjecture. In the measles outbreak in the Faeroes investigated by Panum (1939), for instance, it is highly improbable that any latent virus was present before the epidemic began. For all the cases were traceable to other cases, and isolated households remained free until contact with cases was established. On the other hand, in a large town the virus may well survive from one epidemic to the next in a few individuals scattered here and there.

Before influenza epidemics, only a few members of the population can very well carry latent virus, for in the pandemic of 1918 isolated islands escaped. In the Samoa group, for instance, the American island of Pago Pago remained free because a strict quarantine was imposed, but the islands of

Upolu and Savaii were almost certainly infected by the steamer *Talune*. In the Falkland Islands epidemic of 1935 it was observed that settlements which had been warned by telephone isolated themselves immediately and escaped infection, so that in time "the island could be divided into sharply defined areas where the disease was or was not present" (Cheverton, 1937). In the pandemic of 1889 Parsons (1891) observed that deep-sea fishermen and lighthouse keepers did not become infected so long as they remained isolated. Thus it would appear that if latent virus plays much part in the genesis of epidemics of influenza it is only in very isolated pockets.

In the common cold, on the other hand, it would seem that latent virus must be quite widespread during interepidemic periods, in view of the unanimity with which the populations of whole countries, and even continents, appear to become infected with the advent of cold weather in the autumn.

Thus, if it be allowed that an epidemic starts as a mobilization of the latent virus in isolated pockets of the population, there must in addition be case-to-case transfer of the virus in order to account for the large number of secondary cases which quickly appear. This transfer, moreover, must occur with great rapidity and very easily.

The path by which viruses travel from person to person is quite unknown, but it may for the present be assumed that the same mechanism operates as in the bacterial infections. In consequence, it may be postulated that the recipient inhales virus particles which have reached free air from the patient either by direct expulsion from the nasopharynx or from buccal or nasal secretions which have dried on his person or surrounding objects.

Expulsion of Viruses

Direct study of the expulsion of virus particles is a difficult proceeding, and, so far as we are aware, has not yet been attempted. If, however, as few virus particles are expelled as are streptococci by cases or by carriers of that organism, and particularly if they follow the same path after expulsion, the difficulty in visualizing direct mouth-to-mouth transfer is equally great. It may well be that, in view of the copious secretion from the nose in a cold and its tendency to increase in measles and influenza, there are many more virus particles available for expulsion, and that, besides being present in the nose, these particles occur in the anterior region of the mouth instead of being mainly confined to the tonsillar region, as appears to be the case with carriers of bacteria. For this reason the expulsion of easily recognizable organisms by normal subjects whose anterior mouth flora had been increased many times by taking up 5 ml. of a suspension of *B. prodigiosus* in saline (the whole of the growth on an agar slope after 24 hours' incubation being employed) was studied in the same manner as with the carriers of streptococci.

The results are given in Table III, from which it will be seen that the artificially infected mouth expels many more organisms than the normal, the majority of them being the indicator organisms. The contrast between such a person and the streptococcal carrier is very marked indeed. Nevertheless, the same general principles apply. The great majority fall downwards out of harm's way, and, even with the larger numbers of organisms available, only by the more violent methods would it be possible to infect the nasopharynx of another person on the same level and only 12 in. (30 cm.) away. This may possibly explain the failure of attempted transmission of influenza during the 1918 epidemic. It is possible, however, that in view of the increase in the number of available organisms, infected droplet nuclei may be commoner than in the bacterial infections.

Table III.—*Average Number of Colonies per Person Isolated Before and After Instillation of B. prodigiosus Culture into the Mouth*

Position of Culture Plate	Talking		Coughing		Blowing		Sneezing	
	Before prodigiosus Total Cols.	After prodigiosus Prodigiosus Only	Before prodigiosus Total Cols.	After prodigiosus Prodigiosus Only	Before prodigiosus Total Cols.	After prodigiosus Prodigiosus Only	Before prodigiosus Total Cols.	After prodigiosus Prodigiosus Only
0° ..	14·2	114·0	1·1	1·0	1·3	14·3	400	400
22·5° ..	18·3	62·5	2·1	4·4	1·6	16·3	400	1,080
45° ..	3·8	16·4	11·8	16·6	8·0	42·3	1,424	2,096
67·5° ..	2·0	4·1	19·6	113·5	29·0	250·0	1,920	1,200
90° ..	0·3	0·7	2·5	4·7	12·0	87·3	1,028	348
Total ..	38·6	197·7	35·1	140·2	51·9	410·2	5,172	6,124
Number of subjects	9		9		3		1	

Contamination of Person and Surroundings

Whether patients with virus infections of the nasopharynx can contaminate their person and surrounding objects has not been determined experimentally, but mere observation of a person in the throes of an acute cold should convince even the most sceptical that the virus is distributed over most of his person and surroundings. There is probably less contamination in influenza, but the prodromal stage of measles may be equally severe. For this reason the following experiments were performed.

Normal subjects had about 1 ml. of a suspension of *B. prodigiosus* instilled into their nostrils four times in the course of an hour and, by the application of soap or small quantities of sneeze-powder, the condition of the nose was made to resemble in some degree that of a person with a cold. The same subjects, but on different days, took cultures into their mouths (twice in the course of an hour) and on other occasions into both nose and mouth. While in this condition they wore a sterilized laboratory coat with pieces of sterile lint, 1 in. (2.5 cm.) square, pinned on in various strategic situations. They then proceeded to carry on with their ordinary occupations around the laboratory.

After an hour the patches were removed, placed into phials containing 5 ml. of broth, and, after shaking, 1/2 ml. of broth in each phial was spread over the surface of a well-dried agar plate. After incubation of the plates for 48 hours at 26° C. the number of *B. prodigiosus* colonies was determined. This figure was multiplied by ten to account for the dilution, giving the total population on 1 sq. in. (6.45 sq. cm.).

Immediately after the removal of the lint squares the coat was taken into a room 8 ft. (244 cm.) by 7 ft. (213 cm.) and 9 ft. 6 in. (290 cm.) high in which seven agar plates were disposed—two on the floor, two on stools 2 ft. (60 cm.) high, two on the bench 2 ft. 6 in. (75 cm.) high, and one on the window-sill 3 ft. (90 cm.) from the floor. The coat was then shaken twice with only moderate vigour. The room was now shut up and left for one hour. The plates were then covered, incubated for 48 hours, and the number of colonies of *B. prodigiosus* determined. For control purposes a similar series of plates were exposed for one hour before the experiment. The room was carefully washed and aired between each experiment.

From Table IV, in which the results are given, it is obvious that when the nose contains many organisms, even for a short period of time, they have no difficulty in reaching and contaminating the clothing of the subject during the ordinary activities of the day. When the organisms are only in the mouth there is rather less contamination. On the clothing being shaken in a small room there was detectable contamination of the air by the indicator organisms. The results varied somewhat with the subject, the clothing of subject A being more heavily contaminated, while the air of a small room contained more organisms.

Table IV.—*Contamination of Laboratory Coats by Normal Subjects after Instillation of B. prodigiosus Culture into Nasopharynx, and Extent of Contamination of the Air of a Small Room after Shaking the Coat*

Site	Subject A							Subject B					
	B. prodigiosus instilled into:							B. prodigiosus instilled into:					
	Nose Only	Nose and Mouth	Mouth Only a	b	c	d	e	Nose Only	Nose and Mouth	Mouth Only a	b	c	d
	No. of prodigiosus on 1 sq. in. (6·45 sq. cm.)							No. of prodigiosus on 1 sq. in. (6·45 sq. cm.)					
R. lapel ..	500	1,400	0	30	0	1,000	0	0	0	0	0	0	20
L. lapel ..	0	20	280	330	0	0	0	0	1,360	0	0	40	20
R. sleeve ..	210	0	0	20	30	0	30	0	0	0	0	0	10
L. sleeve ..	40	0	10	550	0	10	0	30	0	0	0	0	0
R. abdomen	0	80	0	340	20	70	20	20	0	0	0	0	0
L. abdomen	660	50	0	180	20	230	20	0	140	0	0	0	0
Back ..	0	0	0	20	0	10	0	370	0	0	0	0	0
Handkerchief	10,240	—	—	—	—	—	—	—	—	—	—	—	—
	No. of prodigiosus collected on 7 Culture Plates exposed in Room for 1 hour After Shaking Coat:												
	4	8	1	1	4	3	4	4	4	1	1	0	0

It must, however, be borne in mind that in these experiments the subjects were under observation for only one hour, that the organisms instilled into the nasopharynx very quickly disappear, and that the amount of nasal excretion was usually much less than that met with in acute infections. For these reasons the actual number of organisms detected is probably much smaller than the number of virus particles which might have been picked up had the individuals been clinically infected and a suitable technique been available for isolation of the virus.

Mechanism of Transfer from Person to Person

The experiments in the preceding sections show that if the number and location of virus particles in the nasopharynx of a patient in the acute phase of infection bear any resemblance to the number and location of the indicator organisms used in these experiments, the path they follow when travelling from donor to recipient is probably very similar to that followed by the bacteria under consideration in the first part of this paper, the indirect route by way of contamination of the person's clothing and surrounding objects probably being more important than direct mouth-to-mouth transmission.

Consideration, however, of the epidemiology of these infections shows that the release into the atmosphere of the concentrated output over several hours—an apparent prerequisite for the production of further cases of bacterial infection—is by no means necessary in the case of the viruses. For it is hardly necessary to do more than refer to the extremely rapid spread of colds and influenza following their introduction into islands and other isolated communities, while it would be possible to quote several instances from Panum which demonstrate the exceedingly slight contact necessary for the dissemination of measles. It is probable that this is due to a much greater output of infectious particles by persons with acute virus infections, aided by the fact that the virus is present in the nose. For this reason, not only do the surroundings become very heavily contaminated but also the atmosphere in the neighbourhood as well.

There is even a possibility that the person and clothing of others in the vicinity of the patient may become polluted either by droplets falling thereon direct from the patient or by virus particles released into the atmosphere after the buccal and nasal secretions on the person or bedding of the patient have dried. Such persons may become temporary "carriers" in the sense that the virus is on their clothing and not in their throats. In this condition they may convey infection to others at a distance. There is some epidemiological evidence in support of this.

While investigating an outbreak of influenza A in Alaska in 1935 two passengers and a pilot left Fairbanks on April 8 by aeroplane for Kotzebue, where they stayed for several days. The former place had had influenza since Jan. 15, and the latter was in the throes at the time of their arrival. They then proceeded by plane to Point Barrow, arriving on April 15. The Eskimos there became infected, though none of the travellers was infected in any way (Pettit, Mudd, and Pepper, 1936).

During the influenza epidemic in the Falkland Islands in 1935 the supply ship, S.S. *Lafonia*, left Port Stanley on Aug. 30, two members of its crew having been landed on Aug. 28 sick with influenza. "The hands themselves all seemed fit except for slight colds." On Sept. 2 she touched at a port in West Falkland, where "an epidemic of influenza broke out and spread to each place visited by the mail officer from the ship" (Cheverton, 1937).

Isolated communities such as Spitsbergen (Paul and Freese, 1933), Tristan da Cunha (Barrow, 1936), or the settlements in the Arctic north of Canada have very little respiratory infection so long as they remain isolated from civilization, but when contact with the outside world is re-established, usually by boat, the inhabitants suffer from severe colds. As a rule no information is given as to the state of the immigrants, although it may be assumed that they had had contact with colds some time previously. Hirsch (1883), however, mentions that they are usually free of infection at the time of arrival, and Heinbecker and Irvine-Jones (1928), describing an expedition to Baffin Land, mention that "it was not necessary for any member of the expedition to have an acute respiratory infection for the malady to appear amongst the natives."

A third instance may be quoted from the Reverend K. Macauley (1764), who landed on St. Kilda in a spirit of scepticism that healthy people could carry colds, but to his immense surprise colds duly made their appearance amongst the islanders three days later. The same author mentions that some of His Majesty's soldiers landed on Hirta, "and although the natives gave them no manner of assistance" (which was not surprising, for it was the year of Culloden), "at the same time, it is certain . . . that the cold described above attacked them with immense fury."

In the case of measles somewhat similar evidence may be cited from Panum (1939).

"Three weeks before Whitsunday, the provincial surgeon was summoned to Kvalvig, where a severe epidemic of Krujm̃ was prevailing, and he had to spend the night in the village. In the house in which the surgeon slept the measles broke out exactly 14 days after his arrival. No other occasion than his visit could be assigned for the outbreak of the disease, since no resident of Kvalvig had been in any suspected place, and particularly none of those who lived in the house that was first attacked, and since no other stranger from any affected or suspected places had been in the village. . . . To Midtvaag, in Vaagø, the measles came, so people said, with the midwife, who had passed several days with the measles patients at Steegaard. The woman had had the disease herself in Denmark. In all the houses in which the midwife had been, they said, the measles appeared 14 days later; and a girl who washed the midwife's clothes immediately after her arrival was the first who took the measles in Midtvaag."

Thus an aeroplane with three individuals on board, coming from an infected locality, and a mailman from a presumably infected ship, conveyed influenza; the arrival of ships with no apparent infection and the landing of an uninfected clergyman and a party of uninfected soldiers were followed by outbreaks of common colds; and the visit of a surgeon and a midwife, both free from infection themselves but from infected localities, caused measles in other communities. It is arguable that the immigrants were carriers and infected the new community, not necessarily by direct mouth-to-mouth transmission of the virus but indirectly by way of their clothing. If carriers of viruses have no more particles available for distribution than have carriers of streptococci the transmission of virus may be very difficult to achieve without very close and intimate contact. For this reason the alternative suggestion is equally plausible—that the virus was present on the boat or amongst the belongings of the travellers owing to contact with previous cases, and that a sufficient number of particles were released when the clothes were shaken or luggage was unpacked in the new community to cause infections amongst any susceptibles present. In this connexion the observation by Marshall, the surgeon of Shackleton's expedition, that after the party had been completely isolated for many months and was free of infection an outbreak of catarrh followed the opening of a new bale of blankets, is of some importance.

Thus it would seem probable that the person-to-person transfer of virus particles may occur if violent methods of expulsion are employed, but that an indirect route in which the buccal and nasal secretions dry on the person and surrounding objects and reach the atmosphere by shaking, etc., is more probable. Whatever the mechanism may be, there can be little doubt that it is extraordinarily efficient and that, in contrast to the bacterial infections, minimal degrees of contact are all that are necessary. Indeed, the virus may be conveyed to others separated in time and space by considerable distances.

Discussion

It is not suggested that anything more than a working hypothesis has been put forward to account for the spread of the infections under consideration, and it is possible that as further evidence is obtained it may have to be modified or even abandoned altogether. It would seem, however, that the methods by which both bacterial and virus infections are disseminated are essentially similar.

The former evidently requires the slow building up of the carrier rate, and not until a sufficient number of carriers have been assembled can actual clinical infections appear. The virus infections, on the other hand, probably require the presence of individuals carrying virus in the latent form. The frequency with which such persons occur in the population is still a matter for speculation. When the external conditions are right (and what these conditions may be we do not know, though weather may play its part) the virus is mobilized, producing clinically recognizable infection.

In the transfer of infection from person to person, it would seem that much the same mechanism is at work in both bacterial and virus infections. Probably little infection is transferred direct from mouth to mouth, the majority of secondary infections being produced by bacteria or viruses which have followed a circuitous route. In the case of bacterial infections, possibly because very few infectious particles are expelled, this occurs only when the concentrated output over several hours can be suddenly released into the atmosphere. But in the virus infections, possibly because more infectious particles are present, such concentration is unnecessary and infection can be transferred with extreme ease and as a result of only slight degrees of contact.

In view of this the prevention of virus infections by ultraviolet light or aerosols may prove to be extremely difficult, whereas it may be much easier in the case of bacterial infections. This should be borne in mind before expensive installations are contemplated.

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AMPHETAMINE AND CAFFEINE CITRATE IN ANOXAEMIA

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Binet and Strumza (1939a, 1939b) showed that the very large doses of amphetamine of 0.2–0.4 mg. per gramme of body weight delayed the onset of unconsciousness in anoxaemic guinea-pigs, and also that doses of a similar order revived dogs which were comatose from the same cause. In another series of experiments they found that, although caffeine citrate did not increase a dog's resistance to anoxaemia, as measured by the time of onset of unconsciousness, both ephedrine and amphetamine did so, but excessive doses of the latter augmented the depression brought on by oxygen lack. In men, however, who were breathing an oxygen–nitrogen mixture which simulated climbing from an altitude of 10,000 ft. to about 24,000 ft. (3,000–7,300 m.) in 40 minutes, Knehr (1940) and others were unable to demonstrate any improvement in coding and calculating after subcutaneous injections of 20 mg. of amphetamine.

Early in the recent war it became necessary to investigate the actions of amphetamine (benzedrine: Menley and James) and caffeine upon anoxaemia, and a small-scale attempt was made, therefore, to link up a study of the objective performance of anoxaemic airmen with a survey of their symptoms in order to give a double assessment to the action of these two drugs.

Method

In the present investigation five pilots and one ground instructor (who soon afterwards became a pilot) were the subjects for the test on performance, and six pilots and two ground instructors for the experiment on the symptomatology. The nature and purpose of the tests were carefully explained to every man, and it was pointed out that it was no part of the investigation to make them ill, and that they were to mention anything untoward which they noticed. At the same time, however, care was taken not to suggest any of the possible symptoms of anoxaemia either by telling them what to notice or by direct question afterwards.

The test used was to keep a Link, or instrument flying trainer, on an even keel and a set course for 45 minutes when it was going through the motions of an aircraft flying in bumpy air. This machine is the standard synthetic training device for teaching instrument or blind flying in the R.A.F., and it forms one of the nearest copies of real flying which can be numerically scored. It is fitted with the same controls and dashboard instruments as a real aircraft, and can assume the positions of a machine which is climbing, diving, banking, or turning. Movements of the controls, moreover, cause corresponding changes in the attitude of the fuselage and in the readings of the blind-flying instruments. There is also a mechanism which makes the machine assume rapid changes in attitude like those of an aircraft which is flying in rough or bumpy air, and it was considered that the continuous correction of these deflections (which were constant in number and amplitude from test to test) provided a suitable task for an experiment of this kind. The errors in making these corrections were measured by three mechanical integrators (one for each dimension) which gave numerical readings upon three dials, and which were all driven by the same constant-speed electric motor. This mechanism automatically stopped every two minutes, and it took about a minute to note the readings and reset the dials to zero, so that repeated samples of the performance could therefore be obtained at three-minute intervals.

The subjects were made anoxaemic by breathing, through a standard Service telephonist's gas-mask (Fig. 1), an oxygen–

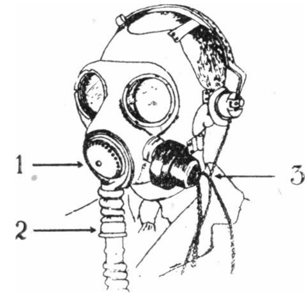

FIG. 1.—Subject wearing Service telephonist's gas-mask. 1, Expiratory valve. 2, Mica valve, closing on expiration. 3, Microphone.

nitrogen mixture containing 11% of the former, which represents an altitude of about 16,200 ft. (5,000 m.). Gas of this composition was fed from large cylinders through a reducing valve and flowmeter into a 10-litre breathing-bag which was slung from the side of the trainer (Fig. 2). A standard time

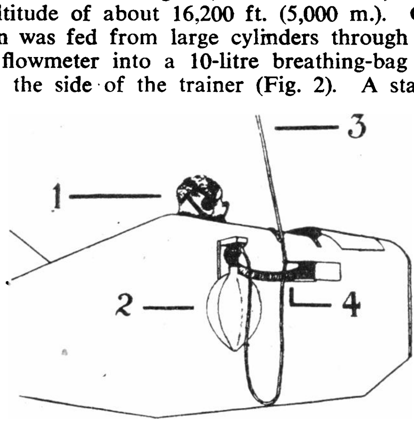

FIG. 2.—Link trainer fuselage with breathing apparatus. 1, Subject in telephonist's gas-mask. 2, 10-litre self-collapsing breathing-bag. 3, Supply pipe from gas cylinders. 4, Flexible rubber hose to mask.

of five minutes was taken to change over from breathing air to this mixture. The mask was fitted with a microphone and connected to the breathing-bag by a piece of wide-bore corrugated hose-pipe, and in its base was a light mica valve which shut on expiration, and which was fitted in such a position as to